APPENDIX 2

I hereby certify that this correspondence is being filed via EFS-Web with the United States Patent and Trademark Office on June 5, 2009

TOWNSEND and TOWNSEND and CREW LLP

By: Shirley Hale

PATENT
Attorney Docket No.: 018891-004310US

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:

Senter, et al.

Application No.: 10/522,911

Filed: July 7, 2005

For: DRUG CONJUGATES AND THEIR USE FOR TREATING CANCER, AN AUTOIMMUNE DISEASE OR AN INFECTIOUS DISEASE

Customer No.: 51535

Confirmation No.: 7034

Examiner: Christina Bradley

Technology Center/Art Unit: 1654

DECLARATION UNDER 37 C.F.R. § 1.132 AND *In re Katz*

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

We, Peter Senter, Brian Toki, and Svetlana Doronina, hereby declare as follows:

1) That we, Peter Senter, Brian Toki, and Svetlana Doronina, have reviewed the above-identified application, application number 10/522,911, the original claim set of application number 10/522,911, the pending claim set of application number 10/522,911, and the amended claim set provided in Appendix A.

2) That we, Peter Senter, Brian Toki, and Svetlana Doronina, are the sole co-inventors of the subject matter set forth in the original, pending and amended claim sets.

3) That we, Peter Senter, Brian Toki, and Svetlana Doronina, are co-authors of a published abstract of the oral presentation entitled "Cures and Regressions of Established Tumor Xenografts with Monoclonal Antibody Auristatin E Conjugates" which was cited as item C12 in

the Information Disclosure Statement filed with the U.S. Patent and Trademark Office on July 7, 2005 for the above-identified U.S. Patent Application.

4) That Brian Toki presented slides and gave the oral presentation associated with the abstract entitled "Cures and Regressions of Established Tumor Xenografts with Monoclonal Antibody Auristatin E Conjugates" which was presented at the 223rd National Meeting of the American Chemical Society, held during April 7-11, 2002, in Orlando, Florida. Copies of the slides were not publicly distributed at that meeting.

5) That to the extent that the subject matter disclosed and claimed in the original, pending or amended claim set is also disclosed in the published abstract, oral presentation or slides, we three (Peter Senter, Brian Toki, and Svetlana Doronina) are the sole co-inventors of said subject matter disclosed therein.

6) That to the extent said published abstract, oral presentation or slides describe antibody-drug conjugates comprising Auristatin E (AE), Auristatin E benzoylvaleric acid ester (AEVB), Monomethyl Auristatin E (MMAE), or Auristatin E paraacetyl benzoic acid ester (AEB), we three (Peter Senter, Brian Toki, and Svetlana Doronina) are the sole co-inventors of said subject matter.

7) That the other eight co-authors of the published abstract, Charles (Chuck) Cerveny, Dana Chace, Joe Francisco, Kerry Klussman, Brian Mendelsohn, Damon Meyer, Jennifer Thompson and Alan Wahl, although co-authors of the published abstract, are not co-inventors of the subject matter claimed in the original, pending or amended claim set and are not co-inventors of the subject matter presented in said published abstract, oral presentation or slides.

8) That the nine individuals acknowledged in the slides accompanying the oral presentation, Charles (Chuck) Cerveny, Dana Chace, Joe Francisco, Kerry Klussman, Brian Mendelsohn, Damon Meyer, Jennifer Thompson, Alan Wahl and Tim Bovee, although acknowledged in the slides accompanying the oral presentation, are not co-inventors of the subject matter claimed in the original, pending or amended claim set and are not co-inventors of the subject matter presented in said published abstract, oral presentation or slides.

We further declare that all statements made herein of our own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under §1001 of Title 18 of the United

States Code, and that such willful false statements may jeopardize the validity of the above identified patent application or any patent issuing thereon.

Dated: 6/2/09

Peter Senter

Dated: 6/2/09

Brian Toki

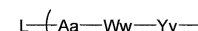
Dated: 6/2/2009

Svetlana Doronina

62038570 v1

APPENDIX A

1. (Currently amended) A compound of the Formula Ia:



Ia

or a pharmaceutically acceptable salt thereof

wherein,

L- is a Ligand unit;

-A- is a Stretcher unit;

a is 1;

each -W- is independently an Amino Acid unit;

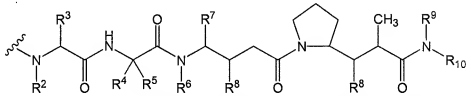
-Y- is a self-immolative Spacer unit;

w is an integer ranging from 2 to 12;

y is 1 or 2;

p ranges from 1 to about 20; and

-D is a Drug unit of the formula



wherein, the wavy line indicates the point of attachment to the Spacer unit, and independently at each location:

R^2 is selected from **the group consisting of** -H and -C_1-C_8 alkyl;

R^3 is selected from **the group consisting of** -H, -C_1-C_8 alkyl, -C_3-C_8 carbocycle, -O-(C_1-C_8 alkyl), -aryl, -C_1-C_8 alkyl-aryl, -C_1-C_8 alkyl-(C_3-C_8 carbocycle), -C_3-C_8 heterocycle and -C_1-C_8 alkyl-(C_3-C_8 heterocycle);

R^4 is selected from **the group consisting of** -H, -C_1-C_8 alkyl, -C_3-C_8 carbocycle, -O-(C_1-C_8 alkyl), -aryl, -C_1-C_8 alkyl-aryl, -C_1-C_8 alkyl-(C_3-C_8 carbocycle), -C_3-C_8 heterocycle and -C_1-C_8 alkyl-(C_3-C_8 heterocycle) wherein R^5 is selected from **the group consisting of** -H and -methyl; or R^4 and R^5 join and form a ring with the carbon atom to which they are attached

and R^4 and R^5 have the formula $-(CR^aR^b)_n-$ wherein R^a and R^b are independently selected from **the group consisting of** -H, $-C_1$-C_8 alkyl and $-C_3$-C_8 carbocycle and n is selected from **the group consisting of** 2, 3, 4, 5 and 6;

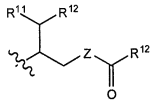
R^6 is selected from **the group consisting of** -H and $-C_1$-C_8 alkyl;

R^7 is selected from **the group consisting of** -H, $-C_1$-C_8 alkyl, $-C_3$-C_8 carbocycle, -O-(C_1-C_8 alkyl), -aryl, $-C_1$-C_8 alkyl-aryl, $-C_1$-C_8 alkyl-(C_3-C_8 carbocycle), $-C_3$-C_8 heterocycle and $-C_1$-C_8 alkyl-(C_3-C_8 heterocycle);

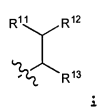
each R^8 is independently selected from **the group consisting of** -H, -OH, $-C_1$-C_8 alkyl, $-C_3$-C_8 carbocycle and -O-(C_1-C_8 alkyl);

R^9 is selected from **the group consisting of** -H and $-C_1$-C_8 alkyl;

R^{10} is selected from **the group consisting of:**



and



;

Z is -O-, -S-,-NH- or $-N(R^{14})-$;

R^{11} is selected from **the group consisting of** -H, -OH, $-NH_2$, $-NHR^{14}$, $-N(R^{14})_2$, $-C_1$-C_8 alkyl, $-C_3$-C_8 carbocycle, -O-(C_1-C_8 alkyl), -aryl, $-C_1$-C_8 alkyl-aryl, $-C_1$-C_8 alkyl-(C_3-C_8 carbocycle), $-C_3$-C_8 heterocycle and $-C_1$-C_8 alkyl-(C_3-C_8 heterocycle); or R^{11} is an oxygen atom which forms a carbonyl unit (C=O) with the carbon atom to which it is attached and a hydrogen atom on this carbon atom is replaced by one of the bonds in the (C=O) double bond;

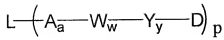
each R^{12} is independently selected from **the group consisting of** -aryl and $-C_3$-C_8 heterocycle;

R^{13} is selected from **the group consisting of** -H, -OH, $-NH_2$, $-NHR^{14}$, $-N(R^{14})_2$, $-C_1$-C_8 alkyl, $-C_3$-C_8 carbocycle, -O-(C_1-C_8 alkyl), -aryl, $-C_1$-C_8 alkyl-aryl, $-C_1$-C_8 alkyl-(C_3-C_8 carbocycle), C_3-C_8 heterocycle and $-C_{1-8}$ alkyl-(C_3-C_8 heterocycle); and

each R^{14} is independently -H or $-C_1$-C_8 alkyl.

2-6. (Canceled)

7. (Currently amended) A compound of the formula Ia:



Ia

or a pharmaceutically acceptable salt thereof

wherein,

L- is a Ligand unit;

-A- is a Stretcher unit;

a is 1;

each -W- is independently an Amino Acid unit;

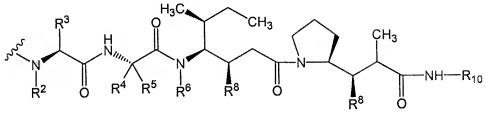
-Y- is a self-immolative Spacer unit;

w is an integer ranging from 2 to 12;

y is 1 or 2;

p ranges from 1 to about 20; and

-D is a Drug unit having the structure



or a pharmaceutically acceptable salt thereof,

wherein, the wavy line is the point of attachment to the Spacer unit, and

independently at each location:

R^2 is selected from **the group consisting of** -H and -methyl;

R^3 is selected from **the group consisting of** -H, -methyl, and -isopropyl;

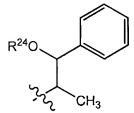
R^4 is selected from **the group consisting of** -H and -methyl;

R^5 is selected from **the group consisting of** -isopropyl, -isobutyl, -sec-butyl, -methyl and -t-butyl or R^4 and R^5 join, and form a ring with the carbon atom to which they are attached and R^4 and R^5 have the formula $-(CR^aR^b)_n-$ where R^a and R^b are independently selected from **the group consisting of** -H, $-C_1$-C_8 alkyl, and $-C_3$-C_8 carbocycle, and n is selected from **the group consisting of** 2, 3, 4, 5 and 6;

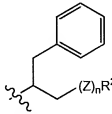
R^6 is selected from **the group consisting of** -H and -methyl;

each R^8 is independently selected from **the group consisting of** -OH, -methoxy and -ethoxy;

R^{10} is selected from **the group consisting of:**



and



R^{24} is selected from **the group consisting of** H and $-C(O)R^{25}$-; wherein R^{25} is selected from **the group consisting of** $-C_1-C_8$ alkyl, $-C_3-C_8$ carbocycle, -aryl, $-C_1-C_8$ alkyl-aryl, $-C_1-C_8$ alkyl-(C_3-C_8 carbocycle), $-C_3-C_8$ heterocycle and $-C_1-C_8$ alkyl-(C_3-C_8 heterocycle);

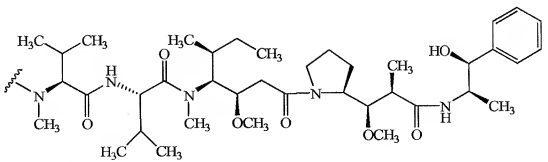
Z is -O-, -NH-, -OC(O)-, -NHC(O)-, **or** $-NR^{28}C(O)$-; where R^{28} is selected from **the group consisting of** -H and $-C_1-C_8$ alkyl;

n is 0 or 1; and

R^{27} is selected from **the group consisting of** -H, $-N_3$, $-C_1-C_8$ alkyl, $-C_3-C_8$ carbocycle, -aryl, $-C_1-C_8$ alkyl-aryl, $-C_1-C_8$ alkyl-(C_3-C_8 carbocycle), $-C_3-C_8$ heterocycle and $-C_1-C_8$ alkyl-(C_3-C_8 heterocycle) when n is 0; and R^{27} is selected from **the group consisting of** -H, $-C_1-C_8$ alkyl, $-C_3-C_8$ carbocycle, -aryl, $-C_1-C_8$ alkyl-aryl, $-C_1-C_8$ alkyl-(C_3-C_8 carbocycle), $-C_3-C_8$ heterocycle and $-C_1-C_8$ alkyl-(C_3-C_8 heterocycle) when n is 1.

8. (Canceled)

9. (Currently amended) A compound or a pharmaceutically acceptable salt of the compound of claim 1 where -D is a Drug unit having the structure:



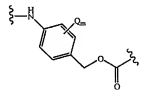
10-16. (Canceled)

17. (Currently amended) A compound or a pharmaceutically acceptable salt of the compound of claim 1 **or claim 7** where**in** the Ligand unit is an antibody.

18. (Currently amended) The compound or a pharmaceutically acceptable salt of the compound of claim 17 where the antibody ~~**unit**~~ is a monoclonal antibody.

19. (Currently amended) The compound or a pharmaceutically acceptable salt of the compound of claim 18 where the monoclonal antibody specifically binds the CD30 antigen, ~~**the CD70 antigen,**~~ the CD20 antigen, ~~**or**~~ the Lewis **X or Y** antigen**, the CD33 antigen, the CD38 antigen, the CEA antigen, the CD19 antigen, the CA15-3 antigen or the epidermal growth factor antigen**.

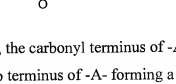
20. (Currently amended) The compound or a pharmaceutically acceptable salt of the compound of claim 1 where -Yy- is



Q is selected from **the group consisting of** -C_1-C_8 alkyl, -O-(C_1-C_8 alkyl), -halogen, -nitro and -cyano; and

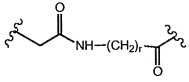
m is an integer ranging from 0-4, the amino terminus of -Yy- forming a bond with the Amino acid unit and the ~~**carboxyl**~~ **other** terminus of -Yy- forming a bond with the Drug unit.

21. (Previously presented) The compound or a pharmaceutically acceptable salt of the compound of claim 1 where -A- is



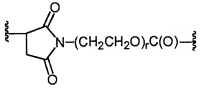
and r is an integer ranging from 1-10, the carbonyl terminus of -A- forming a bond with the Amino Acid unit and the succinimido terminus of -A- forming a bond with the Ligand unit.

22. (Withdrawn) The compound or a pharmaceutically acceptable salt of the compound of claim 1 where -A- is



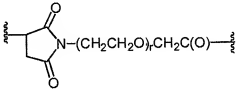
and r is an integer ranging from 1-10, the carbonyl terminus of -A- forming a bond with the Amino Acid unit and the amidomethyl terminus of -A- forming a bond with the Ligand unit.

23. (Withdrawn) The compound or a pharmaceutically acceptable salt of the compound of claim 1 where -A- is



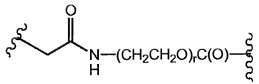
and r is an integer ranging from 1-10, the carbonyl terminus of -A- forming a bond with the Amino acid unit and the succinimido terminus of -A- forming a bond with the Ligand unit.

24. (Withdrawn) The compound or a pharmaceutically acceptable salt of the compound of claim 1 where -A- is



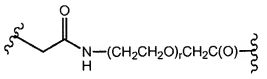
and r is an integer ranging from 1-10, the carbonyl terminus of -A- forming a bond with the Amino acid unit and the succinimido terminus of -A- forming a bond with the Ligand unit.

25. (Withdrawn) The compound or a pharmaceutically acceptable salt of the compound of claim 1 where -A- is



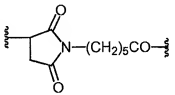
and r is an integer ranging from 1-10, the carbonyl terminus of -A- forming a bond with the Amino acid unit and the amidomethyl terminus of -A- forming a bond with the Ligand unit.

26. (Withdrawn) The compound or a pharmaceutically acceptable salt of the compound of claim 1 where -A- is



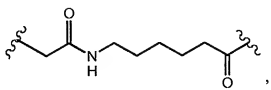
the carbonyl terminus of -A- forming a bond with the Amino acid unit and the amidomethyl terminus of -A- forming a bond with the Ligand unit.

27. (Previously presented) The compound or a pharmaceutically acceptable salt of the compound of claim 21 where -A- is



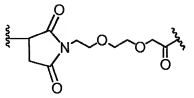
the carbonyl terminus of -A- forming a bond with the Amino acid unit and the succinimido terminus of -A- forming a bond with the Ligand unit.

28. (Withdrawn) The compound or a pharmaceutically acceptable salt of the compound of claim 22 where -A- is



the carbonyl terminus of -A- forming a bond with the Amino acid unit and the amidomethyl terminus of -A- forming a bond with the Ligand unit.

29. (Withdrawn) The compound or a pharmaceutically acceptable salt of the compound of claim 24 where -A- is

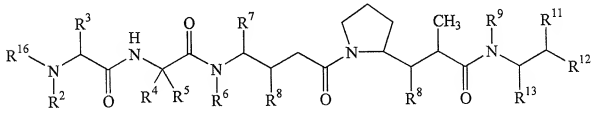


the carbonyl terminus of -A- forming a bond with the Amino acid unit and the succinimido terminus of -A- forming a bond with the Ligand unit.

30. (Withdrawn) The compound or a pharmaceutically acceptable salt of the compound of claim 1 where -W_w- is -Phenylalanine-Lysine-, the amino terminus of -W_w- forming a bond with the Stretcher unit and the C- terminus of -W_w-forming a bond with the Spacer unit.

31-43. (Canceled)

44. (Currently amended, Withdrawn) A compound of the formula



or a pharmaceutically acceptable salt thereof

wherein, independently at each location:

R^2 is selected from **the group consisting of** -H and -C_1-C_8 alkyl;

R^3 is selected from **the group consisting of** -H, -C_1-C_8 alkyl, -C_3-C_8 carbocycle, -O-(C_1-C_8 alkoxy), -aryl, -C_1-C_8 alkyl-aryl, -C_1-C_8 alkyl-(C_3-C_8 carbocycle), -C_3-C_8 heterocycle and -C_1-C_8 alkyl-(C_3-C_8 heterocycle);

R^4 is selected from **the group consisting of** -H, -C_1-C_8 alkyl, -C_3-C_8 carbocycle, -O-(C_1-C_8 alkoxy), -aryl, -C_1-C_8 alkyl-aryl, -C_1-C_8 alkyl-(C_3-C_8 carbocycle), -C_3-C_8 heterocycle and -C_1-C_8 alkyl-(C_3-C_8 heterocycle) wherein R^5 is selected from **the group consisting of** -H and -methyl; or R^4 and R^5 join and form a ring with the carbon atom to which they are attached and R^4 and R^5 have the formula -$(CR^aR^b)_n$- wherein R^a and R^b are independently selected from **the group consisting of** -H, -C_1-C_8 alkyl and -C_3-C_8 carbocycle and n is selected from **the group consisting of** 2, 3, 4, 5 and 6;

R^6 is selected from **the group consisting of** -H and -C_1-C_8 alkyl;

R^7 is selected from **the group consisting of** -H, -C_1-C_8 alkyl, -C_3-C_8 carbocycle, -O-(C_1-C_8 alkoxy), -aryl, -C_1-C_8 alkyl-aryl, -C_1-C_8 alkyl-(C_3-C_8 carbocycle), -C_3-C_8 heterocycle and -C_1-C_8 alkyl-(C_3-C_8 heterocycle);

each R^8 is independently selected from **the group consisting of** -H, -OH, -C_1-C_8 alkyl, -C_3-C_8 carbocycle and -O-(C_1-C_8 alkoxy);

R^9 is selected from **the group consisting of** -H and -C_1-C_8 alkyl;

R^{11} is selected from **the group consisting of** -H, -OH, -NH_2, -NHR^{14}, -$N(R^{14})_2$, -C_1-C_8 alkyl, -C_3-C_8 carbocycle, -O-(C_1-C_8 alkyl), -aryl, -C_1-C_8 alkyl-aryl, -C_1-C_8 alkyl-(C_3-C_8 carbocycle), -C_3-C_8 heterocycle and -C_1-C_8 alkyl-(C_3-C_8 heterocycle); or R^{11} is an oxygen atom which forms a carbonyl unit (C=O) with the carbon atom to which it is attached and a hydrogen atom on this carbon atom is replaced by one of the bonds in the (C=O) double bond;

each R^{12} is independently selected from **the group consisting of** -aryl and -C_3-C_8 heterocycle;

R^{13} is selected from **the group consisting of** -H, -OH, -NH_2, -NHR^{14}, -$N(R^{14})_2$, -C_1-C_8 alkyl, -C_3-C_8 carbocycle, -O-(C_1-C_8 alkoxy), -aryl, -C_1-C_8 alkyl-aryl, -C_1-C_8 alkyl-(C_3-C_8 carbocycle), -C_3-C_8 heterocycle and -C_1-C_8 alkyl-(C_3-C_8 heterocycle);

each R^{14} is independently -H or -C_1-C_8 alkyl;

R^{16} is A'a-Ww-Yy-

wherein

each -W- is independently an Amino Acid unit;

-Y- is a self-immolative Spacer unit;

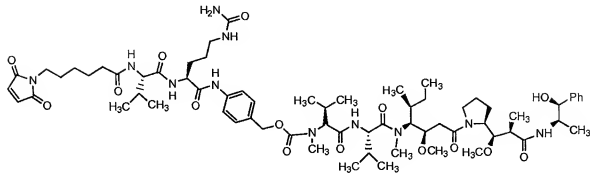
w is an integer ranging from 2 to 12;

y is 1 or 2;

-A' is a Stretcher unit; and

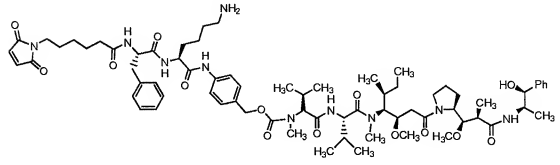
a is 1.

45. (Withdrawn) The compound of claim 44 having the structure



or a pharmaceutically acceptable salt thereof.

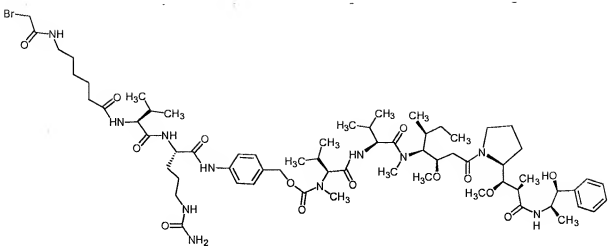
46. (Withdrawn) The compound of claim 44 having the structure



or a pharmaceutically acceptable salt thereof.

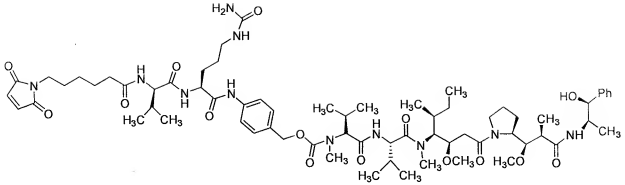
47. (Canceled)

48. (Withdrawn) The compound of claim 44 having the structure

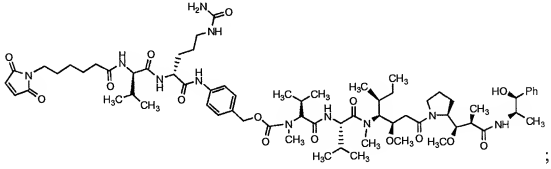


or a pharmaceutically acceptable salt thereof.

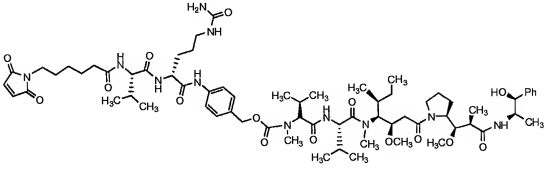
49. (Withdrawn) The compound of claim 44 having the structure



;



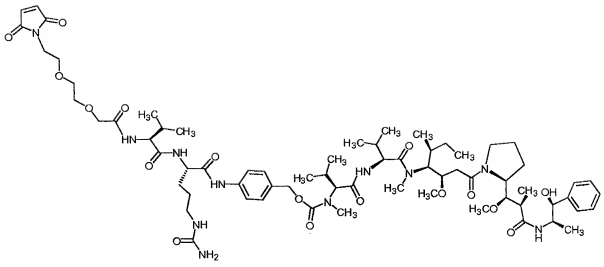
; or



or a pharmaceutically acceptable salt thereof.

50-51. (Canceled)

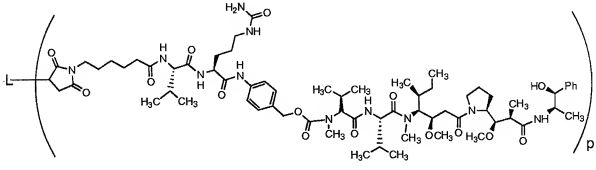
52. (Withdrawn) The compound of claim 44 having the structure



or a pharmaceutically acceptable salt thereof.

53. (Canceled)

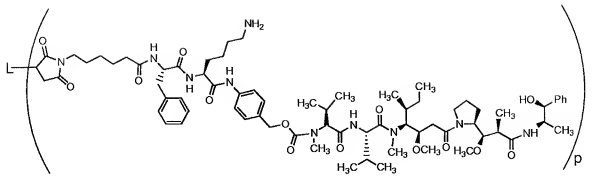
54. (Currently amended) The compound of claim **[[1]]<u>128</u>** having the structure



~~**where p ranges from 1 to about 20**~~, or a pharmaceutically acceptable salt thereof.

55. (Canceled)

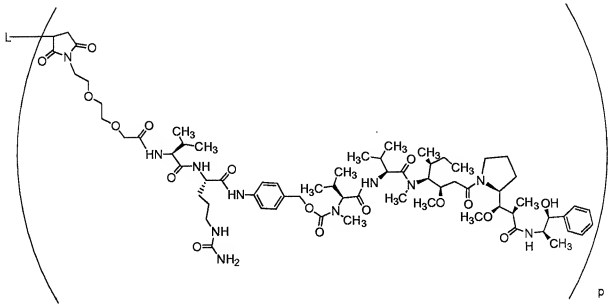
56. (Withdrawn) The compound of claim 1 having the structure



where p ranges from 1 to about 20, or a pharmaceutically acceptable salt thereof.

57-58. (Canceled)

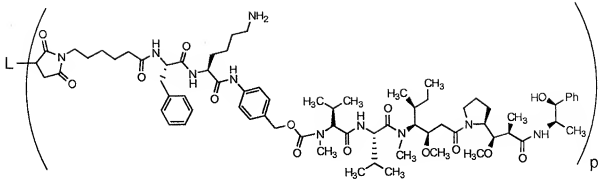
59. (Withdrawn) The compound of claim 1 having the structure



where p ranges from 1 to about 20, or a pharmaceutically acceptable salt thereof.

60-76. (Canceled)

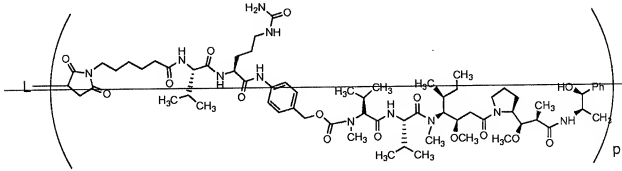
77. (Currently amended, Withdrawn) The compound of claim 1 having the formula



or a pharmaceutically acceptable salt thereof, ~~where p ranges from about 1 to about 8 and~~**wherein** L is a monoclonal antibody.

78. (Canceled)

79. (Currently amended) The compound of claim [[1]]**54** ~~having the formula~~



or a pharmaceutically acceptable salt thereof, ~~where p ranges from about 1 to about 8 and~~**wherein** L is a monoclonal antibody.

80-99. (Canceled)

100. (Withdrawn) The compound or pharmaceutically acceptable salt thereof of claim 79 wherein L specifically binds the CD20 antigen.

101-103. (Canceled)

104. (Withdrawn) The compound or pharmaceutically acceptable salt thereof of claim 77 wherein L specifically binds the CD20 antigen.

105-110. (Canceled)

111. (Currently amended) A composition comprising an effective amount of a compound or a pharmaceutically acceptable salt thereof of claim 1 **or claim 7,** and a pharmaceutically acceptable carrier or vehicle.

112-118. (Canceled)

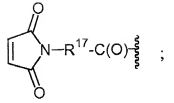
119. (Previously presented) The compound or a pharmaceutically acceptable salt thereof of claim 1 in an isolated or a purified form.

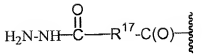
120. (Canceled)

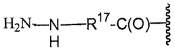
121. (Previously presented) The compound or a pharmaceutically acceptable salt of the compound of claim 1 where -W_w- is -valine-citrulline-, the amino terminus of -W_w- forming a bond with the Stretcher unit, and the C- terminus of -W_w- forming a bond with a the Spacer unit.

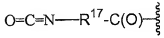
122. (Currently amended, Withdrawn) The compound of claim 44 or a pharmaceutically acceptable salt of the compound of claim 44, wherein

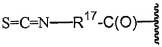
-A' is selected from **the group consisting of:**

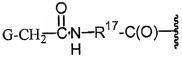

;

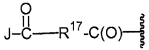

;

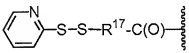

;

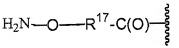

;


;


;


;


; and


;

wherein

G is selected from **the group consisting of** -Cl, -Br, -I, -O-mesyl and -O-tosyl;

J is selected from **the group consisting of** -Cl, -Br, -I, -F, -OH, -O-N-succinimide, -O-(4-nitrophenyl), -O-pentafluorophenyl, -O-tetrafluorophenyl and -O-C(O)-OR^{18};

a is 1;

R^{17} is selected from **the group consisting of** -C_1-C_{10} alkylene-, -C_3-C_8 carbocyclo-, -O-(C_1-C_8 alkoxy)-, -arylene-, -C_1-C_{10} alkylene-arylene-, -arylene-C_1-C_{10} alkylene-, -C_1-C_{10} alkylene-(C_3-C_8 carbocyclo)-, -(C_3-C_8 carbocyclo)-C_1-C_{10} alkylene-, -C_3-C_8 heterocyclo-, -C_1-C_{10} alkylene-(C_3-C_8 heterocyclo)-,
-(C_3-C_8 heterocyclo)-C_1-C_{10} alkylene-, -$(CH_2CH_2O)_r$-, and -$(CH_2CH_2O)_r$-CH_2-;

r is an integer ranging from 1-10; and

R^{18} is -C_1-C_8 alkyl or -aryl.

123. (Canceled)

124. (Previously presented) A composition comprising an effective amount of a compound or a pharmaceutically acceptable salt thereof of claim 79 and a pharmaceutically acceptable carrier or vehicle.

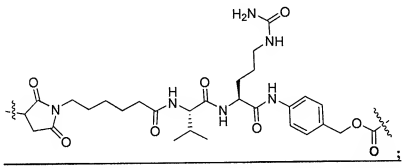
125. (Previously presented) A composition comprising an effective amount of a compound or a pharmaceutically acceptable salt thereof of claim 121 and a pharmaceutically acceptable carrier or vehicle.

126. (Previously presented) The compound or a pharmaceutically acceptable salt thereof of claim 79 in an isolated or a purified form.

127. (Previously presented) The compound or a pharmaceutically acceptable salt thereof of claim 121 in an isolated or a purified form.

128. (Currently Amended) ~~The compound of claim 56 where p ranges from about 1 to about 8~~ **The compound or a pharmaceutically acceptable salt of the compound of claim 1 wherein**

-Aa-Ww-Yy- has the formula:

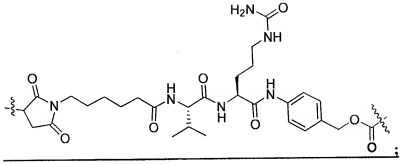


;

the succinimido terminus forming a bond with the Ligand unit and the other terminus forming a bond with the Drug unit.

129. (Currently Amended) ~~The compound of claim 59 where p ranges from about 1 to about 8~~ **The compound or a pharmaceutically acceptable salt of the compound of claim 7 wherein**

-Aa-Ww-Yy- has the formula:



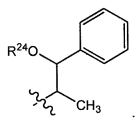
;

the succinimido terminus forming a bond with the Ligand unit and the other terminus forming a bond with the Drug unit.

130. (Currently Amended) ~~The compound of claim 63 where p ranges from about 1 to about 8~~ The compound or a pharmaceutically acceptable salt of the compound of claims 128 or 129 wherein the ligand unit is a monoclonal antibody

131. (Previously presented) The compound or pharmaceutically acceptable salt thereof of claim 1 where R^{10} is

132. (Previously presented) The compound or pharmaceutically acceptable salt thereof of claim 7 where R^{10} is

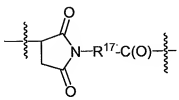


133. (New) The compound or a pharmaceutically acceptable salt of the compound of claim 19 wherein the monoclonal antibody specifically binds the CD30 antigen.

134. (New) The compound or a pharmaceutically acceptable salt of the compound of claim 19 wherein the monoclonal antibody specifically binds the CD19 antigen

135. (New) The compound or a pharmaceutically acceptable salt of the compound of claim 19 wherein the monoclonal antibody specifically binds the CD33 antigen.

136. (New) The compound or a pharmaceutically acceptable salt of the compound of claim 1 wherein -A_a- is



wherein R^{17} is selected from the group consisting of -C_1-C_{10} alkylene, C_3-C_8 carbocyclo-, -O-(C_1-C_8 alkyl)-, -arylene-, -C_1-C_{10} alkylene-arylene-, -arylene-C_1-C_{10} alkylene-, -C_1-C_{10} alkylene-(C_3-C_8 carbocyclo)-, -(C_3-C_8 carbocyclo)-C_1-C_{10} alkylene-, -C_3-C_8 heterocyclo-, -C_1-C_{10} alkylene-(C_3-C_8 heterocyclo)-, - (C_3-C_8 heterocyclo)-C_1-C_{10}alkylene-, -$(CH_2CH_2O)_r$-, and -$(CH_2CH_2O)_r$-CH_2-; and r is an integer ranging from 1-10.

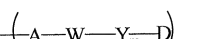
137. (New) A compound or a pharmaceutically acceptable salt of the compound of claim 1 wherein p ranges from 1 to about 5.

138. (New) A compound or a pharmaceutically acceptable salt of the compound of claim 79 wherein p ranges from 1 to about 5.

139. (New) A compound or a pharmaceutically acceptable salt of the compound of claim 54 where L is a monoclonal antibody that specifically binds the CD30 antigen, the CD20 antigen, the Lewis antigen, the CD33 antigen, the CD19 antigen, the CD38 antigen, the CEA antigen, the CA15-3 antigen or the epidermal growth factor antigen.

140. (New) A compound or a pharmaceutically acceptable salt of the compound of claim 139 wherein the monoclonal antibody specifically binds the CD30 antigen.

141. (New) A composition comprising drug-linker-ligand conjugates having Formula Ia:



Ia

or a pharmaceutically acceptable salt thereof;

wherein,

L- is a Ligand unit;

-A- is a Stretcher unit;

a is 1;

each -W- is independently an Amino Acid unit;

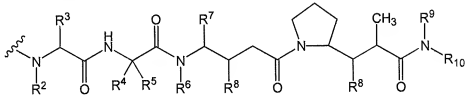
-Y- is a self-immolative Spacer unit;

w is an integer ranging from 2 to 12;

y is 1 or 2;

p ranges from 1 to about 5 and is the average number of $-A_a-W_w-Y_y-D$ units per ligand in the composition; and

-D is a Drug unit of the formula



wherein, the wavy line indicates the point of attachment to the Spacer unit, and independently at each location:

R^2 is selected from the group consisting of -H and $-C_1-C_8$ alkyl;

R^3 is selected from the group consisting of -H, $-C_1-C_8$ alkyl, $-C_3-C_8$ carbocycle, $-O-(C_1-C_8$ alkyl), -aryl, $-C_1-C_8$ alkyl-aryl, $-C_1-C_8$ alkyl-(C_3-C_8 carbocycle), $-C_3-C_8$ heterocycle and $-C_1-C_8$ alkyl-(C_3-C_8 heterocycle);

R^4 is selected from the group consisting of -H, $-C_1-C_8$ alkyl, $-C_3-C_8$ carbocycle, $-O-(C_1-C_8$ alkyl), -aryl, $-C_1-C_8$ alkyl-aryl, $-C_1-C_8$ alkyl-(C_3-C_8 carbocycle), $-C_3-C_8$ heterocycle and $-C_1-C_8$ alkyl-(C_3-C_8 heterocycle) wherein R^5 is selected from the group consisting of -H and -methyl; or R^4 and R^5 join and form a ring with the carbon atom to which they are attached and R^4 and R^5 have the formula $-(CR^aR^b)_n-$ wherein R^a and R^b are independently selected from the group consisting of -H, $-C_1-C_8$ alkyl and $-C_3-C_8$ carbocycle and n is selected from the group consisting of 2, 3, 4, 5 and 6;

R^6 is selected from the group consisting of -H and $-C_1-C_8$ alkyl;

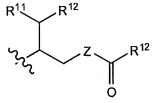
R^7 is selected from the group consisting of -H, $-C_1-C_8$ alkyl, $-C_3-C_8$ carbocycle, $-O-(C_1-C_8$ alkyl), -aryl,

-C_1-C_8 alkyl-aryl, -C_1-C_8 alkyl-(C_3-C_8 carbocycle), -C_3-C_8 heterocycle and -C_1-C_8 alkyl-(C_3-C_8 heterocycle);

each R^8 is independently selected from the group consisting of -H, -OH, -C_1-C_8 alkyl, -C_3-C_8 carbocycle and -O-(C_1-C_8 alkyl);

R^9 is selected from the group consisting of -H and -C_1-C_8 alkyl;

R^{10} is selected from the group consisting of:



and

Z is -O-, -S-,-NH- or -N(R^{14})-;

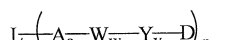
R^{11} is selected from the group consisting of -H, -OH, -NH_2, -NHR^{14}, -N(R^{14})$_2$, -C_1-C_8 alkyl, -C_3-C_8 carbocycle, -O-(C_1-C_8 alkyl), -aryl, -C_1-C_8 alkyl-aryl, -C_1-C_8 alkyl-(C_3-C_8 carbocycle), -C_3-C_8 heterocycle and -C_1-C_8 alkyl-(C_3-C_8 heterocycle); or R^{11} is an oxygen atom which forms a carbonyl unit (C=O) with the carbon atom to which it is attached and a hydrogen atom on this carbon atom is replaced by one of the bonds in the (C=O) double bond;

each R^{12} is independently selected from the group consisting of -aryl and -C_3-C_8 heterocycle;

R^{13} is selected from the group consisting of -H, -OH, -NH_2, -NHR^{14}, -N(R^{14})$_2$, -C_1-C_8 alkyl, -C_3-C_8 carbocycle, -O-(C_1-C_8 alkyl), -aryl, -C_1-C_8 alkyl-aryl, -C_1-C_8 alkyl-(C_3-C_8 carbocycle), C_3-C_8 heterocycle and -C_{1-8} alkyl-(C_3-C_8 heterocycle); and

each R^{14} is independently -H or -C_1-C_8 alkyl.

142. (New) A composition comprising drug-linker-ligand conjugates having Formula Ia:



Ia

or a pharmaceutically acceptable salt thereof

wherein,

L- is a Ligand unit;

-A- is a Stretcher unit;

a is 1;

each -W- is independently an Amino Acid unit;

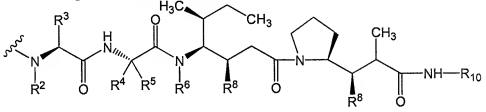
-Y- is a self-immolative Spacer unit;

w is an integer ranging from 2 to 12;

y is 1 or 2;

p ranges from 1 to about 5 and is the average number of $-A_a-W_w-Y_y-D$ units per ligand in the composition; and

-D is a Drug unit having the structure



or a pharmaceutically acceptable salt thereof,

wherein, the wavy line is the point of attachment to the Spacer unit, and

independently at each location:

R^2 is selected from the group consisting of -H and -methyl;

R^3 is selected from the group consisting of -H, -methyl, and -isopropyl;

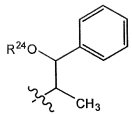
R^4 is selected from the group consisting of -H and -methyl;

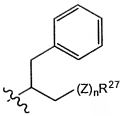
R^5 is selected from the group consisting of -isopropyl, -isobutyl, -sec-butyl, -methyl and -t-butyl or R^4 and R^5 join, and form a ring with the carbon atom to which they are attached and R^4 and R^5 have the formula $-(CR^aR^b)_n-$ where R^a and R^b are independently selected from the group consisting of -H, $-C_1-C_8$ alkyl, and $-C_3-C_8$ carbocycle, and n is selected from the group consisting of 2, 3, 4, 5 and 6;

R^6 is selected from the group consisting of -H and -methyl;

each R^8 is independently selected from the group consisting of -OH, -methoxy and -ethoxy;

R^{10} is selected from the group consisting of:



and


R^{24} is selected from the group consisting of H and -C(O)R^{25}-; wherein R^{25} is selected from the group consisting of -C_1-C_8 alkyl, -C_3-C_8 carbocycle, -aryl, -C_1-C_8 alkyl-aryl, -C_1-C_8 alkyl-(C_3-C_8 carbocycle), -C_3-C_8 heterocycle and -C_1-C_8 alkyl-(C_3-C_8 heterocycle);

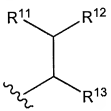
Z is -O-, -NH-, -OC(O)-, -NHC(O)-, or -NR^{28}C(O)-; where R^{28} is selected from the group consisting of -H and -C_1-C_8 alkyl;

n is 0 or 1; and

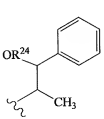
R^{27} is selected from the group consisting of -H, -N_3, -C_1-C_8 alkyl, -C_3-C_8 carbocycle, -aryl, -C_1-C_8 alkyl-aryl, -C_1-C_8 alkyl-(C_3-C_8 carbocycle), -C_3-C_8 heterocycle and -C_1-C_8 alkyl-(C_3-C_8 heterocycle) when n is 0; and

R^{27} is selected from the group consisting of -H, -C_1-C_8 alkyl, -C_3-C_8 carbocycle, -aryl, -C_1-C_8 alkyl-aryl,
-C_1-C_8 alkyl-(C_3-C_8 carbocycle), -C_3-C_8 heterocycle and -C_1-C_8 alkyl-(C_3-C_8 heterocycle) when n is 1.

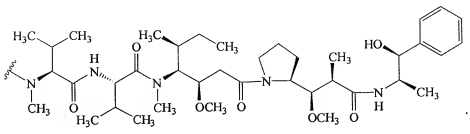
143. (New) The composition of claim 141 wherein R^{10} is



144. (New) The composition of claim 142 wherein R^{10} is



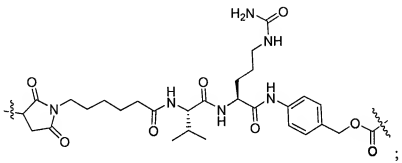
145. (New) The composition of claim 141 where -D is a Drug unit having the structure



;

or a pharmaceutically acceptable salt thereof.

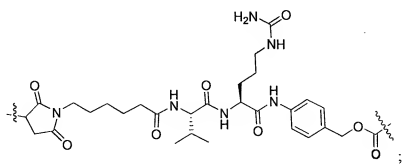
146. (New) The composition of claim 141 wherein -Aa-Ww-Yy- has the formula:



;

the succinimido terminus forming a bond with the Ligand unit and the other terminus forming a bond with the Drug unit.

147. (New) The composition of claim 142 wherein -Aa-Ww-Yy- has the formula:



;

the succinimido terminus forming a bond with the Ligand unit and the other terminus forming a bond with the Drug unit.

148. (New) The composition of claim 141 where the ligand unit is a monoclonal antibody.

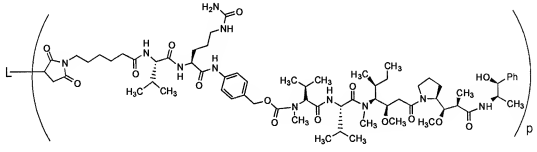
149. (New) The composition of claim 148 wherein the monoclonal antibody specifically binds the CD30 antigen, the CD20 antigen, the CD19 antigen, the Lewis antigen, the CD33 antigen, the CD38 antigen, the CEA antigen, the CA15-3 antigen or the epidermal growth factor antigen.

150. (New) The composition of 149 wherein the monoclonal antibody specifically binds the CD19 antigen

151. (New) The composition of claim 149 wherein the monoclonal antibody specifically binds the CD30 antigen.

152. (New) The composition of claim 149 wherein the monoclonal antibody specifically binds the CD33 antigen.

153. (New) The composition of claim 147 wherein the drug-linker-ligand conjugates have the formula:



or a pharmaceutically acceptable salt thereof.

154. (New) The composition of claim 153 wherein L is a monoclonal antibody.

155. (New) The compositon of claim 154 wherein the monoclonal antibody specifically binds the CD20 antigen, the CD30 antigen, the CD33 antigen, the CD19 antigen, the CD38 antigen, the CA15-3 antigen, the CEA antigen, or the epidermal growth factor antigen.

156. (New) The compositon of claim 155 wherein the monoclonal antibody specifically binds the the CD30 antigen.

157. (New) The composition of claim 155 wherein the monoclonal antibody specifically binds the CD19 antigen

158. (New) The composition of claim 155 wherein the monoclonal antibody specifically binds the CD20 antigen.

159. (New) The composition of claim 155 wherein the monoclonal antibody specifically binds the CD33 antigen.

160. (New) The composition of claim 142 wherein L is a monoclonal antibody.

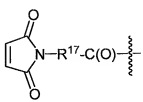
161. (New) The compositon of claim 160 wherein the monoclonal antibody specifically binds the CD20 antigen, the CD30 antigen, the CD33 antigen, the CD19 antigen, the CD38 antigen, the CA15-3 antigen, the CEA antigen, or the epidermal growth factor antigen.

162. (New) The composition of claim 161 wherein the monoclonal antibody specifically binds the CD30 antigen.

163. (New) The composition of claim 154 wherein the antibody is attached to the drug moiety through a cysteine residue of the antibody.

164. (New) The compound of claim 122 or a pharmaceutically acceptable salt of the compound of claim 122, wherein

A_a- is



wherein R^{17} is selected from the group consisting of -C_1-C_{10} alkylene, C_3-C_8 carbocyclo-, -O-(C_1-C_8 alkyl)-, -arylene-, -C_1-C_{10} alkylene-arylene-, -arylene-C_1-C_{10} alkylene-, -C_1-C_{10} alkylene-(C_3-C_8 carbocyclo)-, -(C_3-C_8 carbocyclo)-C_1-C_{10} alkylene-, -C_3-C_8 heterocyclo-, -C_1-C_{10} alkylene-(C_3-C_8 heterocyclo)-, - (C_3-C_8 heterocyclo)-C_1-C_{10}alkylene-, -$(CH_2CH_2O)_r$-, and -$(CH_2CH_2O)_r$-CH_2-; and r is an integer ranging from 1-10.

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